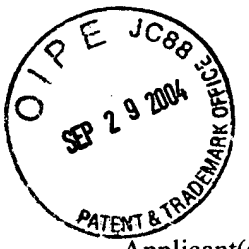
09-30-04

IFW



PATENT
Atty Docket No. 65015
EV525170389US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Chunying Du, et al.	Group No.	1645
Serial No.:	10/730,476	Examiner:	Unknown
Filed:	December 8, 2003	Confirmation No.	3329
For:	Compositions and Methods for Cleaving IAP		

Mail Stop PGPUB
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL

Dear Sir:

Attached please find the following:

☒ Request for Corrected Publication Under 37 CFR 1.221(b);

☒ "Marked Up Version" of pages 84-86 of Published Application No. US 2004/0171105 A1;

☒ Certificate of Mailing by First Class Mail;

☒ Stamped, pre-addressed postcard;

CERTIFICATE OF MAILING

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Cheryl Couzens — Signature

9.29.04 — Date

The Commissioner is hereby authorized to charge any additional fees, which may be required to Deposit Account No. 50-1662. A duplicate of this request is attached.

Respectfully submitted,

POLSINELLI SHALTON WELTE SUELTHAUS PC

Date: September 29, 2004

By: _____

Holly M. Amjad, Reg. No. 41,582
700 W. 47th Street, Suite 1000
Kansas City, Missouri 64112
Tel: (816) 360-4299
Fax: (816) 753-1536
Attorney for Applicants

018538 / 065015
HMAMJ 1132726

CERTIFICATE OF MAILING BY "FIRST CLASS MAIL" (37 CFR 1.8)			Matter No.	
Applicant(s): Chunying Du, et al.			65015	
Serial No.	Filing Date	Examiner	Group Art No.	Confirmation No.
10/730,476	December 8, 2003	Unknown	1645	3329

Invention: COMPOSITIONS AND METHODS FOR CLEAVING IAP

I hereby certify that a Transmittal (2 pages, in duplicate); Request for Corrected Publication Under 37 CFR 1.221(b) (4 pages); "Marked Up Version" of Published US Application No. 2004/0171105 A1 (pages 84, 85 & 86) (3 pgs. total); a Certificate of Mailing by Express Mail 37 CFR 1.10 (1 page); and a stamped, pre-addressed postcard are being mailed by U.S. Postal Service "Express Mail" to Addressee, Mail Stop PGPUB, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, this 29th day of September, 2004.

Cheryl Couzens
(Typed or Printed Name of Person Mailing Correspondence)

Cheryl Couzens
(Signature of Person Mailing Correspondence)

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HMAMJ 1132730

PATENT
Atty Docket No. 65015
EV 525170389 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Chunying Du, et al.	Group No.	1645
Serial No.:	10/730,476	Examiner:	Unknown
Filed:	December 8, 2003	Confirmation No.	3329
For:	Compositions and Methods for Cleaving IAP		

Mail Stop – PGPUB
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P.O. Box 1450
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Request for Corrected Publication Under 37 CFR 1.221(b)

Dear Sir:

A review of publication number U.S. 2004/0171105 (the '105 publication) published on September 2, 2004, revealed numerous material mistakes within the claims section of the application as published which did not appear in the application as filed. Applicant hereby requests that the '105 publication be corrected according to 37 CFR 1.221(b). As previously noted, the '105 publication was published on September 2, 2004, therefore Applicant's request for corrected publication is within the two month time frame required by Rule 1.221(b). The U.S. Patent and Trademark Office (U.S. PTO) made numerous material mistakes throughout the

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Cheryl Couzens
Name of Depositor

Cheryl Couzens
Signature

9.29.04
Date

claims, which affect the interpretation of the claims as published. Applicant describes the material mistakes and indicates where in the specification as originally filed the text appears in the following paragraphs. Since this request is based on U.S. PTO material mistakes under 37 CFR 1.221(b), Applicant does not believe any fees are due at this time.

Applicant, authorizes any charges that may be associated with this request to be made to Deposit Account No. 50-1662, and asks that attorney be notified of any such charges.

Correct Text in the Specification

At page 81 of the specification as filed, lines 12 and 13, in claim 5, reference to SEQ ID NOs. appears on line 12, at the end of line 12, the last number is "11-", the first number on line 13 is "19", thereby indicating SEQ ID NOs. "11-19." In the '105 publication, claim 5 includes a SEQ ID NO "1119", rather than SEQ ID NOs. "11-19."

At page 82 of the specification as filed, lines 14 and 15, in claim 13, reference to SEQ ID NOs. appears on line 14, at the end of line 14, the last number is "11-", the first number on line 15 is "19", thereby indicating SEQ ID NOs. "11-19." In the '105 publication, claim 13 includes a SEQ ID NO "1119", rather than SEQ ID NOs. "11-19."

At page 82 of the specification, line 19, in claim 16, the word "IAP" is used. In the '105 publication, at line 1 of claim 16, the "I" has been replaced by an "L" so that the word becomes "LAP", in the '105 publication. Further, at page 82 of the specification, line 20, in claim 16, the word "IAP" is used. In the '105 publication, at line 3 of claim 16, the "I" has been replaced by an "L" so that the word becomes "LAP", in the '105 publication.

At page 83 of the specification, line 18, in claim 25, the word "IAP" is used. In the '105 publication, at line 3 of claim 25, the "I" has been replaced by an "L" so that the word becomes "LAP", in the '105 publication.

At page 83 of the specification, line 21, in claim 27, the word "IAP" is used twice. In the '105 publication, at line 2 of claim 27, with regards to the second "IAP", the "I" has been replaced by an "L" so that the word becomes "LAP", in the '105 publication.

At page 84 of the specification, line 19, in claim 38, the symbol "$C1_{n1}$" is used. In the '105 publication, at line 1 of claim 38, the subscript "n" is missing so that the symbol referenced becomes "$C1_1$", instead of "$C1_{n1}$".

At page 86 of the specification, line 13, in claim 49, the word "IAP" is used. In the '105 publication, at line 12 of claim 49, the "I" has been replaced by an "L" so that the word becomes "LAP", in the '105 publication.

At page 88 of the specification, line 1 and line 2, in claim 59, the word "IAP" is used. In the '105 publication, at line 2 of claim 59, the "I" has been replaced by an "L" so that the word becomes "LAP" both times it appears on line 2 of claim 59 in the '105 publication.

Remarks

The material mistakes appearing in the '105 publication did not appear in the application as originally submitted to the U.S. PTO. The material mistakes within the claims affect the public's ability to determine the scope of the provisional rights Applicant may seek to enforce once the current application issues as a patent. The material mistakes with regards to the SEQ ID NOs. 11-19 makes it impossible for the public when reviewing claims 5 and 13 of the '105 publication to understand the scope of these claims and the subject matter covered by these claims. With regards to claims 16, 25, 27, 49, and 59, the use of "LAP" instead of "IAP" renders the claims inoperable. Claim 38 as it appears in the '105 publication is also rendered inoperable by the use of the symbol "$C1_1$", instead of the symbol "$C1_{n1}$." Thus, Applicant hereby requests that a corrected publication under 37 CFR 1.221(b) be published. Applicant has included a

marked up version of pages 84, 85, and 86 of the '105 publication indicating Applicant's requested corrections as required by 37 CFR 1.221(b). Applicant believes that based on the text of the specification as originally submitted to the U.S. PTO, the record is clear that the material mistakes were made by the U.S. PTO at the time of publication of the application and therefore should be corrected under 37 CFR 1.221(b).

Respectfully submitted,

POLSINELLI SHALTON WELTE SUELTHAUS PC

Date: September 29, 2004

By: _____

Holly M. Amjad, Reg. No. 41,582
700 W. 47th Street, Suite 1000
Kansas City, Missouri 64112
Tel: (816) 360-4299
Fax: (816) 753-1536
Attorney for Applicants

018538 / 065015
HMAMJ 1132385

-continued

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<400> SEQUENCE: 82

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 83

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What is claimed is:

1. A method for cleaving IAP, wherein the method comprises:

contacting in vitro, isolated IAP with an amount of an isolated Omi family polypeptide, whereby upon contact, the Omi family polypeptide will cleave the IAP.

2. The method of claim 1, wherein the IAP is selected from the group consisting of cIAP1, cIAP2, XIAP, Livin α, Livin β, and DIAP1.

3. The method of claim 1, wherein the Omi family polypeptide is selected from the group consisting of SEQ ID NOs. 44, 45, 48, 49, 54-57, 60-63, 66-75, and homologs thereof.

4. The method of claim 1, wherein the Omi family polypeptide to IAP molar ratio in vitro is equal to between 1:5 to 1:30 molar ratio of Omi to IAP.

5. The method of claim 1, wherein the Omi family polypeptide is expressed by a nucleic acid sequence molecule selected from the group consisting of SEQ ID NOs. 1-3,6-8,1119, 22-27, and 30-39, and homologs thereof.

6. The method of claim 1, wherein the in vitro conditions incubation time is 2 hours at 37° C. in solution.

7. A method for cleaving IAP, wherein the method comprises:

(a) isolating a population of cells, whereby the caspase found in the cells is bound by IAP;

(b) contacting in vitro the isolated cell population with the Omi family polypeptide whereby upon contact, the Omi family polypeptide cleaves the IAP from the caspase.

8. The method of claim 7, wherein the Omi family polypeptide is selected from the group consisting of SEQ ID NOs. 44, 45, 48, 49, 54-57, 60-63, 66-75.

9. The method of claim 7, wherein the Omi family polypeptide is selected from the group consisting of Omi WT, OmiΔPDZ, OmiΔAVPS, Omi protease and Omi catalytic triad.

10. The method of claim 8, wherein the Omi family polypeptide is in a carrier.

11. The method of claim 10, wherein the carrier is a liposome.

12. A method for cleaving IAP comprising:

(a) isolating and amplifying an Omi family member gene;

(b) forming an Omi expression construct from the isolated and amplified Omi family member gene;

(c) transfecting a cell population having caspase bound by IAP, with the Omi family member construct; and,

(d) causing expression of the Omi vector, whereby the OMI family polypeptide cleaves IAP.

13. The method of claim 12, wherein the Omi family polypeptide is expressed by a nucleic acid sequence molecule selected from the group consisting of SEQ ID NOs. 1-3,6-8,1119, 22-27, and 30-39, and homologs thereof.

14. The method of claim 12, wherein expression is caused by the addition of etoposide.

15. The method of claim 12, wherein expression is caused by damage to the cell.

16. A method for cleaving IAP, wherein the method comprises:

contacting isolated IAP with an amount of an isolated Omi family polypeptide, whereby upon contact, the Omi family polypeptide will cleave the IAP.

17. A polypeptide for cleaving IAP selected from the group consisting of Omi WT, OmiΔPDZ, OmiΔAVPS, Omi protease, Omi catalytic triad, and homologs thereof.

18. The polypeptide of claim 17, comprising a carrier.

19. The polypeptide of claim 17, wherein the polypeptide is selected from the group consisting of expressed intracellular, isolated, or recombinant polypeptides.

20. An isolated polypeptide for cleaving IAP selected from the group consisting of SEQ ID NOs. 44, 45, 48, 49, 54-57, 60-63, 66-75, and homologs thereof.

21. A polypeptide for cleaving IAP comprising a protease domain selected from the group consisting of SEQ ID NOs. 64-66 and 75-80, and homologs thereof.

22. A polypeptide having increased protease activity comprising a polypeptide selected from the group consisting of SEQ ID NOs. 48, 49, 55, 56, 57, 60-63, 66-75, and homologs thereof.

23. A polypeptide for binding to a BIR site on an IAP, comprising SEQ ID NO. 77 and homologs thereof.

24. A polypeptide for cleaving IAP comprising a polypeptide selected from the group consisting of SEQ ID NOs. 44 and 45, and homologs thereof.

25. The polypeptide of claim 24, wherein the Omi to IAP molar ratio in vitro is equal to between 1:5 to 1:30 molar ratio of Omi to IAP.

26. A polypeptide which binds to IAP, but does not cleave IAP, selected from the group consisting of SEQ ID NOs. 46, 47, 50, 51, 58, 59, 64, 65, and homologs thereof.

27. A polypeptide which binds IAP but does not cleave IAP comprising Omi SA.

28. An Omi serine protease for use in cleaving IAP.

29. An OmiΔPDZ for cleaving IAP.

30. A polypeptide molecule for cleaving an IAP comprising an amino acid sequence as set forth in $C1_{n1}$-R1-$C2_{n2}$-R2-$C3_{n3}$-R3-$C4_{n4}$, wherein:

(a) R1 is a serine;

(b) R2 is an amino acid residue selected from a group consisting of charged amino acid residues and aromatic amino acid residues;

(c) R3 is an amino acid residue selected from a group consisting of charged amino acid residues and polar amino acid residues; and,

(d) R1, R2 and R3 form a catalytic triad for cleavage of the IAP.

31. The molecule of claim 30, wherein R2 is an amino acid residue selected from a group consisting of histidine, lysine, arginine, phenylalanine, tyrosine, and tryptophan.

32. The molecule of claim 30, wherein R3 is an amino acid residue selected from a group consisting of aspartic acid, glutamic acid, lysine, histidine, and arginine.

33. The polypeptide of claim 30, wherein $C1_{n1}$, $C2_{n2}$, $C3_{n3}$, and $C4_{n4}$ are polypeptide chains.

34. The polypeptide of claim 33, wherein n1 is a number between 10 and 100.

35. The polypeptide of claim 33, wherein n2 is a number between 10 and 100.

36. The polypeptide of claim 33, wherein n3 is a number between 10 and 150.

37. The polypeptide of claim 33, wherein n4 is a number between 10 and 200.

38. The molecule of claim 33, wherein the $C1_1$ chain is the N-terminal and has an AVPS motif sequence that operably couples to IAP.

39. The molecule of claim 33, wherein the $C4_{n4}$ chain is the C-terminal and has a hinge sequence and PDZ domain.

40. The molecule of claim 39, wherein the PDZ domain is removed.

41. The molecule of claim 30 wherein a $C1_{n1}$ polypeptide chain has an N-terminal location and comprises an amino acid sequence as set forth in SEQ ID NOs. 54 and 55.

42. The polypeptide of claim 30 operably enclosed in a liposome in an aqueous medium.

43. A polypeptide molecule comprising an amino acid sequence as set forth in SEQ ID NOs. 54 and 55.

44. A serine protease polypeptide molecule wherein the molecule is of the formula comprising $C1_{n1}$-R1-$C2_{n2}$-R2-$C3_{n3}$-R3-$C4_{n4}$, wherein:

(a) R1 is a serine;

(b) R2 is an amino acid residue selected from a group consisting of a charged amino acid residue and an aromatic amino acid residue;

(c) R3 is an amino acid residue selected from a group consisting of a charged amino acid residue and a polar amino acid residue;

(d) $C1_{n1}$, $C2_{n2}$, $C3_{n3}$, and $C4_{n4}$ are polypeptide chains;

(e) n1 is an amino acid residue number ranging between 10 and 100;

(f) n2 is an amino acid residue number ranging between 10 and 100;

(g) n3 is an amino acid residue number ranging between 10 and 150;

(h) n4 is an amino acid residue number ranging between 10 and 200; and,

(i) R1, R2 and R3 form a catalytic triad for cleavage of a polypeptide substrate.

45. A polypeptide molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 46, 47, and homologs thereof.

46. A polypeptide molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 48, 49 and homologs thereof.

47. A polypeptide molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 56, 57 and homologs thereof.

48. A polypeptide molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NOs. 60 through 63 and homologs thereof.

49. A polypeptide molecule for inhibiting IAP cleavage comprising an amino acid sequence as set forth in $C1_{n1}$-R1-$C2_{n2}$-R2-$C3_{n3}$-R3-$C4_{n4}$, wherein:

(a) R_1 is an amino acid residue selected from a group consisting of an alanine, an arginine, an aspartic acid, an asparagine, a cysteine, a glutamic acid, a glutamine, a glycine, a histidine, an isoleucine, a leucine, a lysine, a methionine, a phenylalanine, a proline, a threonine, a tryptophan, a tyrosine, and a valine;

(b) R_2 is a histidine;

(c) R_3 is an aspartic acid; and,

(d) an AVPS moiety binds to IAP.

50. An OmiΔPDZ expressed intra-cellularly by an OmiΔPDZ vector in a cell.

51. A nucleic acid sequence, which expresses a polypeptide which cleaves IAP, wherein the nucleic acid sequence is

selected from the group consisting of Omi family member nucleic acid sequences, degenerate variants of the Omi family member, and homologous sequences to the Omi family member.

52. The nucleic acid sequence of claim 51, wherein the sequence is selected from the group consisting of SEQ ID NOs. 1-41, and homologos sequences thereof.

53. The nucleic acid sequence of claim 51, wherein the sequence is selected from the group consisting of Omi WT, OmiΔPDZ, OmiΔAVPS, Omi protease, Omi catalytic triad, and homologs thereof.

54. A nucleic acid sequence which expresses isolated polypeptide for cleaving IAP, wherein the nucleic acid sequence is selected from the group consisting of SEQ ID NOs. 1-43, and homologos sequences thereof.

55. A nucleic acid sequence which expresses a polypeptide for cleaving IAP, wherein the nucleic acid sequence expresses a protease domain, selected from the group consisting of SEQ ID NOs. 44, 45, 48 and 49, and homologos sequences thereof.

56. A nucleic acid sequence which expresses a polypeptide having increased protease activity comprising a polypeptide selected from the group consisting of SEQ ID NOs. 48, 49, 50, 56, 57, 58, 59, 60, 61, and homologos sequences thereof.

57. A nucleic acid sequence which expresses a polypeptide for binding to a BIR site on an IAP, comprising SEQ ID NO. 82 and homologos sequences thereof.

58. A nucleic acid sequence which expresses a polypeptide for cleaving IAP comprising a polypeptide selected from the group consisting of SEQ ID NOs. 44, 45, and homologous sequences thereof.

59. A nucleic acid sequence, which expresses a polypeptide, which binds to IAP, but does not cleave IAP, selected from the group consisting of SEQ ID NOs. 4, 5, 9, 10, 20, 21, 28, and 29, and homologs thereof.

60. A nucleic acid sequence which expresses a polypeptide which binds IAP but does not cleave IAP, comprising Omi SA.

61. An expression vector comprising a nucleic acid that expresses a molecule for cleaving IAP selected from a group consisting of SEQ ID NOs. 1-43, and homologous sequences thereof.

62. The expression vector of claim 61, wherein the expression vector is selected from a group consisting of a plasmid and an episome.

63. The expression vector of claim 61, wherein the expression vector comprises a replicating virus.

64. The expression vector of claim 61, wherein the expression vector is a pE721b vector.

65. An Omi expression vector, comprising an Omi family nucleic acid sequence and a vector selected from the group consisting of eukaryotic vectors MSCV, Harvey murine sarcoma virus, pFastBac, pFastBac HT, pFastBac DUAL, pSFV, pTet-Splice, pEUK-C1, pPUR, pMAM, pMAMneo, pBI101, pBI121, pDR2, pCMVEBNA, YACneo, pSVK3, pSVL, pMSG, pCH110, pKK232-8, p3'SS, pBlueBacIII, pCDM8, pcDNA1, pZeoSV, pcDNA3, pREP4, pET21b, pCEP4, and pEBVHis vectors.

66. A transfected cell comprising:

(a) an expression vector that expresses an Omi family member polypeptide; and,

(b) a promoter.

67. The transfected cell of claim 66, wherein the transfected cell is selected from the group consisting of an animal cell and a plant cell.

68. The transfected cell of claim 66, wherein the transfected cell is a tumor cell.

69. The transfected cell of claim 66, wherein the polypeptide is an OmiΔPDZ.

70. The transfected cell of claim 66, wherein the vector is selected from the group consisting of eukaryotic vectors MSCV, Harvey murine sarcoma virus, pFastBac, pFastBac HT, pFastBac DUAL, pSFV, pTet-Splice, pEUK-C1, pPUR, pMAM, pMAMneo, pBI101, pBI121, pDR2, pCMVEBNA, YACneo, pSVK3, pSVL, pMSG, pCH110, pKK232-8, p3'SS, pBlueBacIII, pCDM8, pcDNA1, pZeoSV, pcDNA3, pREP4, pET21b, pCEP4, and pEBVHis vectors.

71. A pharmaceutical composition for treatment of a hyperproliferative disorder in an animal which comprises a pharmacologically acceptable carrier and a therapeutically effective amount of the liposomes containing Omi family member polypeptides of SEQ ID NOs. 44, 45, 48, 49, 52-57, 60-63, and 66-75.

72. A method of treating the hyperproliferative disorder comprising administering an effective amount of the pharmacological composition of claim 71 into an animal.

73. A hybridization kit for detecting an Omi wild-type gene, wherein the kit comprises:

(a) a container; and,

(b) a nucleic acid molecule comprising a nucleotide molecule selected from a group consisting of Omi family nucleic acid sequences.

74. A hybridization kit for detecting an Omi mutant gene, wherein the kit comprises:

(a) a container; and,

(b) a nucleic acid molecule comprising a molecule selected from a group consisting of SEQ ID NOs. 1-41, and homologous sequences thereof.

75. A kit for detecting an Omi gene comprising:

(a) PCR primers spanning an Omi family gene, a positive control; and,

(b) sequencing products.

76. A kit for detecting an Omi polypeptide, wherein the kit comprises:

(a) a container; and,

(b) an antibody derived from polypeptide selected from a group consisting of SEQ ID NOs. 44-77; and homologs thereof.

77. An antibody which binds to the Omi serine.

78. An antibody which binds to a protease.

79. A mammalian cell consisting essentially of:

(a) a cell transfected by an Omi expression vector;

(b) the transfected cell producing an IAP-cleaving molecule selected from the group consisting of said IAP-cleaving molecules; and,

(c) a promoter controlling transcription and the quantity of production of said IAP-cleaving molecule.

80. The mammalian cell of claim 79, wherein, in the transfected cell, the expression vector is autonomously replicating.